

administered before (Fig. 14) or after (Fig. 15) terbutaline. SNAP, a nitric oxide donor molecule, was nebulized for 20 breaths into the airways of 5 methacholine-bronchoconstricted guinea pigs. In each animal a prompt and
5 profound reduction of lung resistance was produced which lasted about 15 minutes (Fig. 16). Thus, inhalation of NO donor compounds can also produce bronchodilation.

Other embodiments of the invention are within the following claims.

10 What is claimed is:

52

1 1. A method for treating or preventing reversible
2 pulmonary vasoconstriction in a mammal, which method
3 comprises identifying a mammal in need of such treatment or
4 prevention, and causing said mammal to inhale a
5 therapeutically-effective concentration of gaseous nitric
6 oxide.

1 2. The method of claim 1, wherein said pulmonary
2 vasoconstriction is acute pulmonary vasoconstriction.

1 3. The method of claim 1 wherein said mammal has or
2 is at risk of developing a clinical condition selected from
3 the group consisting of pneumonia, traumatic injury,
4 aspiration or inhalation injury, fat embolism in the lung,
5 acidosis, inflammation of the lung, adult respiratory
6 distress syndrome, acute mountain sickness, post cardiac
7 surgery acute pulmonary hypertension, persistent pulmonary
8 hypertension of the newborn, perinatal aspiration syndrome,
9 hyaline membrane disease, acute pulmonary thromboembolism,
10 acute pulmonary edema, heparin-protamine reactions, sepsis,
11 hypoxia, asthma, and status asthmaticus.

1 4. The method of claim 1, wherein said pulmonary
2 vasoconstriction is chronic pulmonary vasoconstriction which
3 has a reversible component.

1 5. The method of claim 1, wherein said mammal has
2 or is at risk of developing a clinical condition selected
3 from the group consisting of chronic pulmonary hypertension,
4 bronchopulmonary dysplasia, chronic pulmonary

5 thromboembolism, idiopathic pulmonary hypertension, and
6 chronic hypoxia.

1 6. The method of claim 1, wherein said nitric oxide
2 is inhaled in a predetermined concentration range for at
3 least three minutes.

1 7. The method of claim 1 wherein said concentration
2 is at least 5 ppm.

1 8. The method of claim 1 wherein said concentration
2 is at least 40 ppm.

1 9. The method of claim 1, wherein said concentration
2 is at least 80 ppm.

1 10. The method of claim 7 wherein said concentration
2 is 180 ppm or less.

1 11. A method for diagnosing the reversibility of
2 chronic pulmonary vasoconstriction in a mammal, which method
3 comprises (a) measuring said mammal's PAP, (b) causing said
4 mammal to inhale gaseous nitric oxide for a period of time,
5 and (c) measuring said mammal's PAP during said period.

1 12. The method of claim 1, wherein said gaseous
2 nitric oxide is inhaled as a mixture comprising nitric
3 oxide, oxygen, and nitrogen gases.

1 13. The method of claim 12, wherein said mixture
2 comprises between 20-99% oxygen gas by volume.

1 14. The method of claim 1, wherein said mammal is a
2 human.

1 15. The method of claim 1, wherein said gaseous
2 nitric oxide is inhaled in the absence of tobacco smoke.

Sub B7C
1 ~~16. A method for treating or preventing pulmonary~~
2 ~~vasoconstriction in a mammal, which method comprises causing~~
3 ~~said mammal to inhale a therapeutically-effective amount of~~
4 ~~a nitric oxide-releasing compound.~~

1 2 17. The method of claim 16, wherein said compound
2 is selected from the group consisting of S-nitroso-N-
3 acetylpenicillamine, S-nitrosocysteine, nitroprusside,
4 nitrosoguanidine, glyceryl trinitrate, isoamyl nitrite,
5 inorganic nitrite, azide, and hydroxylamine.

1 3 18. The method of claim 17², wherein said compound
2 is inhaled in an aerosolized form.

1 4 19. The method of claim 18³, wherein said
2 aerosolized form comprises droplets less than 10 μ m in
3 diameter, said droplets comprising said compound in a
4 suitable pharmacologically-acceptable liquid carrier.

1 5 20. The method of claim 19², wherein said compound
2 is inhaled in powder form comprising particles less than
3 10 μ m in diameter.

Sub C2
1 21. The method of claim 16, wherein said mammal is
2 a human.

1 22. A method for treating or preventing
2 bronchoconstriction in a mammal, which method comprises
3 identifying a mammal in need of such treatment or
4 prevention, and causing said mammal to inhale a
5 therapeutically-effective dose of gaseous nitric oxide.

1 23. The method of claim 22, wherein said mammal is
2 a human.

1 24. The method of claim 22, wherein said gaseous
2 nitric oxide is inhaled in the absence of tobacco smoke.

1 25. The method of claim 22, comprising the
2 additional step of, following said inhalation of gaseous
3 nitric oxide, causing said mammal to inhale a
4 therapeutically-effective dose of a bronchodilator compound
5 in liquid or solid form.

1 26. The method of claim 25, wherein said
2 bronchodilator compound is inhaled with a gas mixture
3 comprising nitric oxide.

1 27. The method of claim 25, wherein said
2 bronchodilator compound is a nitric oxide-releasing
3 compound.

1 28. The method of claim 27, wherein said
2 bronchodilator compound is S-nitroso-N-acetylpenicillamine,
3 S-nitrosocysteine, nitroprusside, nitrosoguanidine, glyceryl
4 trinitrate, isoamyl nitrite, inorganic nitrite, azide, or
5 hydroxylamine.

1 29. The method of claim 25, wherein said
2 bronchodilator compound is an anticholinergic agent, a β_2
3 agonist, a methylxanthine, a calcium-channel blocker, a
4 glucocorticoid drug, or cromolyn sodium.

1 30. The method of claim 22, wherein said
2 bronchoconstriction is associated with asthma.

Sub B3
1 ~~31. A method for treating or preventing~~
2 bronchoconstriction in a mammal, which method comprises
3 identifying a mammal in need of such treatment or
4 prevention, and causing said mammal to inhale a
5 therapeutically-effective amount of a nitric oxide-releasing
6 compound.

1 9 32. The method of claim ⁷31, wherein said
2 bronchoconstriction is associated with asthma.

Sub B3
1 ~~33. The method of claim 31, wherein said compound~~
2 is selected from the group consisting of 3-nitroso-N-
3 acetylpenicillamine, S-nitrosocysteine, nitroprusside,
4 nitrosoguanidine, glyceryl trinitrate, isoamyl nitrite,
5 ~~inorganic nitrite, azide, and hydroxylamine.~~

1 10 34. The method of claim ⁷31, wherein said compound
2 is inhaled in an aerosolized form.

1 11 35. The method of claim ¹⁰34, wherein said
2 aerosolized form comprises droplets less than 10 μ m in
3 diameter, said droplets comprising said compound in a
4 suitable biologically-compatible liquid carrier.

1 ¹² 36. The method of claim 31, wherein said compound
2 is inhaled in powder form comprising particles less than
3 10 μ m in diameter.

1 ~~37. The method of claim 31, wherein said mammal is~~
2 ~~a human.~~

Sub B3 1 ~~38. The method of claim 31, wherein said inhalation~~
2 ~~step is preceded by a step comprising causing said mammal to~~
3 ~~inhale a therapeutically-effective amount of gaseous nitric~~
4 ~~oxide.~~

1 39. A method of improving gas exchange in the lungs
2 of a mammal, said method comprising causing said mammal to
3 inhale a therapeutically-effective amount of gaseous nitric
4 oxide.

1 40. The method of claim 39, wherein said mammal is
2 hypoxic.

1 41. The method of claim 40, wherein said mammal is
2 a human suffering from a lung injury.

1 42. The method of claim 39, wherein said inhalation
2 is accomplished in the absence of tobacco smoke.

1 43. The method of claim 39, wherein said nitric
2 oxide is inhaled at a concentration of at least 1 ppm in
3 air, O₂, or an air/O₂ mixture.

Sub B3 1 ~~44. A method of improving gas exchange in the lungs~~
2 ~~of a mammal, said method comprising causing said mammal to~~

3 inhale a therapeutically-effective amount of a nitric oxide-
4 releasing compound.

Sub D5

1 45. The method of claim 44, wherein said nitric
2 oxide-releasing compound is inhaled in a gas comprising at
3 least 1 ppm nitric oxide.

Sub B6

1 ~~46. The method of claim 44, wherein said nitric~~
2 ~~oxide-releasing compound is S-nitroso-N-acetylpenicillamine,~~
3 ~~S-nitrosocysteine, nitroprusside, nitrosoguanidine, glyceryl~~
4 ~~trinitrate, isoamyl nitrite, inorganic nitrite, azide, or~~
5 ~~hydroxylamine.~~

1 47. A method of delivering a pulmonary pharmaco-
2 active compound into the lungs of a mammal, said method
3 comprising causing said mammal to inhale said compound
4 ~~suspended in a gas comprising nitric oxide.~~

1 18 48. The method of claim 17,
2 is inhaled in the form of a liquid aerosolized in said gas.

1 19 49. The method of claim 17,
2 is inhaled in the form of a powder suspended in said gas.

1 20 50. The method of claim 17,
2 is a bronchodilator.

1 21 51. The method of claim 17,
2 is a surfactant.

1 22 52. The method of claim 17,
2 is an antimicrobial drug.

56

23 53. The method of claim 22, wherein said compound
is gentamycin or pentamidine.

Sub D6 54. An inhaler device comprising
a vessel containing pressurized gas comprising at
least 1 ppm nitric oxide;
a housing defining a lumen, said vessel being
attached to said housing to deliver said gas into said
lumen; and
a mechanism for controllably releasing said gas from
said vessel into said lumen;
said lumen being configured to route said released gas into
the respiratory system of a person, and said device weighing
less than approximately 5 kg.

25 55. The device of claim 24, wherein said device
weighs less than approximately 1 kg.

26 56. The device of claim 24, wherein said
pressurized gas additionally comprises N₂.

27 57. The device of claim 24, wherein said lumen
comprises a rebreathing chamber.

28 58. The device of claim 24, wherein said vessel
additionally contains a liquified propellant.

59. An inhaler device comprising
a housing defining (a) a chamber containing an
inhalable pharmaceutically-active agent and (b) a lumen in
communication with said chamber; and

57

5 a vessel containing pressurized gas comprising at
6 least 1 ppm nitric oxide, said vessel having a mechanism for
7 controllably releasing said gas into said chamber, thereby
8 suspending said agent in said released gas; said lumen being
9 configured to route said released gas into the respiratory
10 system of a patient.

1 60. The device of claim 59, wherein said
2 pharmaceutically-active agent comprises a bronchodilator
3 compound in liquid or solid form.

1 61. The device of claim 60, wherein said compound
2 comprises an anticholinergic agent, a β_2 agonist, a
3 methylxanthine, a calcium-channel blocker, a glucocorticoid
4 drug, or cromolyn sodium.

1 62. The device of claim 59, wherein said
2 pharmaceutically-active agent comprises a nitric oxide-
3 releasing compound.

1 63. The device of claim 62, wherein said compound
2 is selected from the group consisting of S-nitroso-N-
3 acetylpenicillamine, S-nitrosocysteine, nitroprusside,
4 nitrosoguanidine, glyceryl trinitrate, isoamyl nitrite,
5 inorganic nitrite, azide, and hydroxylamine.

1 64. The device of claim 59, wherein said
2 pharmaceutically-active agent comprises an antimicrobial
3 agent.

1 65. The device of claim 64, wherein said
2 antimicrobial agent comprises an antibiotic.

1 66. The device of claim 64, wherein said
2 antimicrobial agent comprises pentamidine.

1 67. The device of claim 59, wherein said
2 pharmaceutically-active agent comprises a surfactant
3 suitable for the treatment of hyaline membrane disease.

1 68. The device of claim 59, wherein said vessel
2 also has a mechanism for controllably releasing said gas
3 into said lumen, in a manner that bypasses said chamber.

Sub B7/ 1 ~~69. A device comprising~~
2 a vessel containing a nitric oxide-donor compound
3 suspended in a compressed or liquified propellant gas;
4 a housing defining (a) a port onto which said vessel
5 is mounted and (b) a lumen in communication with said port;
6 and
7 a mechanism for controllably releasing said
8 propellant from said vessel into said lumen, thereby
9 releasing said suspended compound from said vessel into said
10 lumen;
11 said lumen being configured to route said compound suspended
12 in said released propellant into the respiratory system of a
13 person.

1 ³⁰ 70. The device of claim ²⁹ 69, wherein said compound
2 is in powder form.

1 ³¹ 71. The device of claim ²⁹ 69, wherein said compound
2 is dissolved or suspended in a biologically-compatible
3 liquid carrier.

58

Sub B8

1 ~~72. The device of claim 69, wherein said compound~~
2 ~~is S-nitroso-N-acetylpenicillamine, S-nitrosocysteine,~~
3 ~~nitroprusside, nitrosoguanidine, glyceryl trinitrate,~~
4 ~~isoamyl nitrite, inorganic nitrite, azide, or hydroxylamine.~~

1 73. A device comprising
2 a vessel containing a compressed or liquified
3 propellant gas;
4 a housing defining (a) a chamber containing a nitric
5 oxide-donor compound and (b) a lumen in communication with
6 said chamber;
7 a mechanism for controllably releasing said gas from
8 said vessel into said chamber, thereby suspending said
9 compound in said gas;
10 said lumen being configured to route said compound into the
11 ~~respiratory system of a person.~~

Sub B7

1 74. The device of claim 73, wherein said gas
2 comprises nitric oxide gas.

Sub B9

1 ~~75. The device of claim 73, wherein said nitric~~
2 ~~oxide-donor compound is S-nitroso-N-acetylpenicillamine, S-~~
3 ~~nitrosocysteine, nitroprusside, nitrosoguanidine, glyceryl~~
4 ~~trinitrate, isoamyl nitrite, inorganic nitrite, azide, or~~
5 ~~hydroxylamine.~~

Add B10

add 024